Tetrahedron. Vol. 25, pp. 1055 to 1062. Pergamon Press 1969. Printed in Great Britain

SOLVENT EFFECT ON THE AUTOXIDATION OF L-ASCORBIC ACID[1]

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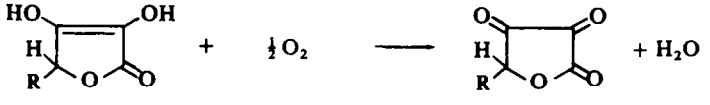
(*Received in Japan* 20 *August* 1968; *Received in the UK for publication* 11 *October* 1968)

Abstract—The kinetics of cupric chloride-catalysed autoxidation of L-ascorbic acid has been studied in a number of organic solvents. The solvent effect can be expressed as a linear function of log k *vs.* reciprocal of dielectric constant ($1/D$) or Reicherdt's empirical parameter of solvent polarity (E_T).[8] The electrical conductance measurement shows that ionization of ascorbic acid to ascorbate ion is affected by the solvent polarity. The stability of ascorbate-copper complex seems to be lower in more polar solvents. The concentration of the complex combined with one or two oxygen molecules is higher at lower temperature. The mechanism of the autoxidation is discussed in comparison with that in aqueous solutions.[2]

ONLY few reports are available concerning the solvent effects on the oxidation of L-ascorbic acid (H_2A), e.g. retardation of enzymatic oxidation in acetic acid[3] and the retardation of copper-catalysed autoxidation in pyridine which forms a complex with cupric ion.[4] The latter solvent effect is similar to the retardation of metaphosphoric acid or N- or S-containing compounds which complex with copper. The rates of oxidation by molecular oxygen,[5] or iodine[6] or potassium permanganate[6] are lowered in the reaction in a solution of alcohol or acetone, and for this no suitable explanation has been offered.

The authors[2] have reported previously the kinetic and mechanistic study of the cupric salt-catalysed autoxidation of L-ascorbic acid to dehydroascorbic acid (DA) in unbuffered aqueous solutions, where R is —$CH(OH)CH_2OH$.



(H_2A) (DA)

The present paper describes the solvent effects on the rate of cupric chloride-catalysed autoxidation, and its relation to the mechanism is discussed.

RESULTS AND DISCUSSION

Autoxidation of ascorbic acid in ethylene glycol. The effect of initial concentrations of ascrobic acid ($[H_2A]_0$), $CuCl_2$ and oxygen on the rate at various reaction temperatures was measured in ethylene glycol as a standard organic solvent. The oxygen consumption curves are similar to those of the reactions in water.[2] Therefore, the reactions in ethylene glycol may also follow Eq. 1. In fact, plots of $\log [H_2A]_0/[H_2A]$ *vs* t give a straight line, where $[H_2A]_0$ and $[H_2A]$ denote the concentrations of

ascorbic acid at time zero and t, respectively. Pseudo-first-order rate constant (k) of Eq. 2 was calculated from the slopes of straight lines. Eq. 2 was also confirmed by UV spectrophotometry described in the Experimental.

$$d[DA]/dt = k[H_2A] \quad (2)$$

The effect of the initial concentration of ascorbic acid is shown in Fig. 1. The decrease of k value with an increase of $[H_2A]_0$ is observed, although the trend is less remarkable than in an aqueous solution. The decrease may be due to the association of the acid or to the transformation of the enolic acid into its keto form and the presence of zeroth-order term in the kinetic equation (the second term in the right side of Eq. 8).[2]

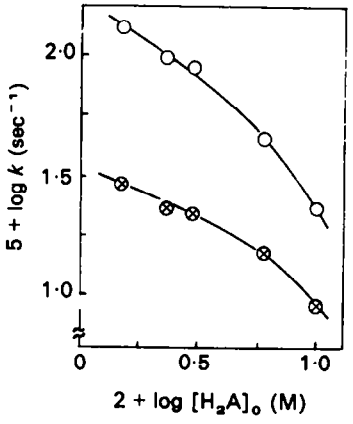


FIG. 1 Effect of initial concentration of ascorbic acid ($[H_2A]_0$) on the rate constants (k) for its autoxidation in the presence of $2{\cdot}3 \times 10^{-4}$M $CuCl_2$ at 25°; ○ in water, ⊗ in ethylene glycol.

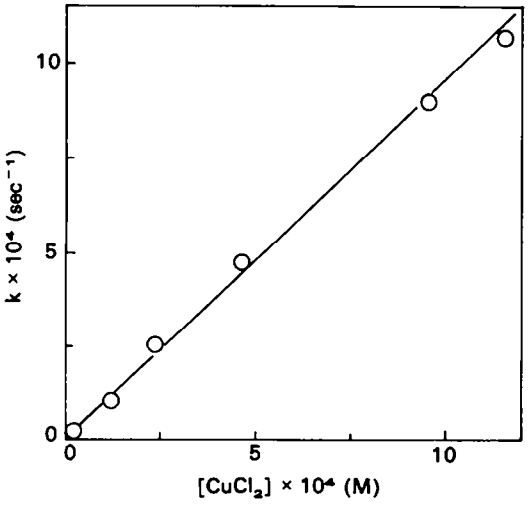


FIG. 2 Effect of $CuCl_2$ concentration on the first-order rate constant for the autoxidation of ascorbic acid ($[H_2A]_0 = 2{\cdot}3 \times 10^{-2}$M) in ethylene glycol at 25°.

The effect of $[CuCl_2]$ in a range of $2{\cdot}3 \times 10^{-5}$–$1{\cdot}1 \times 10^{-3}$M with $2{\cdot}3 \times 10^{-2}$M initial concentration of ascorbic acid ($[H_2A]_0$) is given in Fig. 2. It is obvious that the rate constant k increases proportionally to $[CuCl_2]$ up to $1{\cdot}1 \times 10^{-3}$M or ca. 1/5 times of $[H_2A]_0$. Higher concentration of $CuCl_2$ accelerates the reaction and the saturation of the solution with $CuCl_2$ may cause experimental errors.

These results together with the effect of oxygen pressure and temperature, which will be described later, suggest that the reaction in ethylene glycol may also proceed by Eqs 3–7 as postulated with an aqueous solution.[2]

$$\text{associated } H_2A \rightarrow H_2A \overset{K_3}{\rightleftharpoons} H^+ + HA^- \tag{3}$$

$$HA^- + Cu(II) \overset{K_4}{\rightleftharpoons} [HACu(II)]^- \tag{4a}$$

$$[HACu(II)]^- \overset{k_4}{\rightarrow} HA\cdot + Cu(I) \tag{4b}$$

$$HA^- + Cu(II) + O_2 \overset{K_5}{\rightleftharpoons} [HACu(II)O_2]^- \tag{5a}$$

$$[HACu(II)O_2]^- \overset{k_5}{\rightarrow} HA\cdot + Cu(II) + \cdot O_2^- \tag{5b}$$

$$HA\cdot \underset{+H^+}{\overset{\text{Base}\,(-H^+)}{\rightleftharpoons}} A^{\cdot-} \xrightarrow{Cu(II)} DA + Cu(I) \tag{6}$$

and/or

$$HA\cdot \rightarrow DA\,(+H_2A) \tag{7}$$

General solvent effect. The reaction rates were measured in some other organic solvents, e.g. methanol, n-butanol, aqueous ethanol and dimethylformamide (DMF). Conversion curves at initial stages for various solvents are similar to those in water and in ethylene glycol. Therefore, the rate equation should have the same form as that in an aqueous solution.[2]

$$d[DA]/dt = \frac{3}{2}\frac{K_3[Cu]_T(k_4K_4 + k_5K_5p)}{[H^+]} \times \frac{[H_2A]}{1 + \dfrac{K_3(K_4 + K_5p)[H_2A]}{[H^+]}} \tag{8}$$

Here, $[Cu]_T$ is the total stoichiometric concentration of copper, p is the partial pressure of oxygen, and factor 3/2 corresponds to the effect of hydrogen peroxide produced in the oxidation of cuprous ion to cupric ion or in the reaction of radical anion ($\cdot O_2^-$) with a proton ($\cdot O_2^- + H^+ \rightarrow \cdot O_2H \rightarrow \frac{1}{2}O_2 + \frac{1}{2}H_2O_2$). The concentration of ascorbic acid remaining was estimated by Eq. 1 by means of the oxygen consumption and the concentration was also confirmed by the UV method.[7] This suggests that hydrogen peroxide is consumed according to Eq. 9.

$$\tfrac{1}{2}H_2A + \tfrac{1}{2}H_2O_2 \xrightarrow{\text{fast}} \tfrac{1}{2}DA + H_2O \tag{9}$$

The second term on the right-hand side of Eq. 8, $K_3(K_4 + K_5p)[H_2A]/[H^+]$, may be neglected except at higher concentration of ascorbic acid; plots of log $[H_2A]$ *vs* t gave straight lines, the proportionality of k to $[Cu]_T$ being observed in ethylene glycol (Figs 1 and 2). Eq. 8 can be approximated to Eq. 10.

$$d[DA]/dt = \frac{3}{2}\frac{K_3[Cu]_T(k_4K_4 + k_5K_5p)}{[H^+]}[H_2A] \tag{10}$$

The solvent effect (or polar effect of solvent) on the over-all reaction is presented in Fig. 3 in real lines.

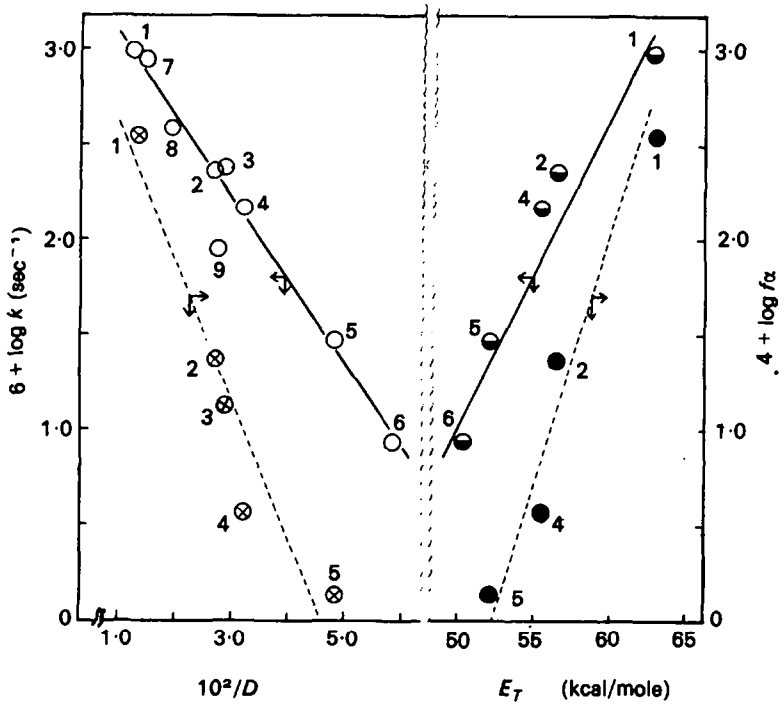


FIG. 3 Relation between rate constant (k) or degree of ionization ($\simeq f\alpha$) and solvent polarity with $[H_2A]_0$ of 2·3 × 10^{-2}M in various solvents at 25°: —○— log k *vs* reciprocal of dielectric constant (D), —⊗— log k *vs.* E_T value, – –⊗– – log $f\alpha$ *vs.* reciprocal of dielectric constant, – –●– – log $f\alpha$ *vs.* E_T value.

1, H_2O; 2, Ethylene glycol; 3, DMF; 4, MeOH; 5, EtOH; 6, n-BuOH; 7, 20% EtOH aq; 8, 50% EtOH aq; 9, 80% EtOH aq.

Dielectric constant (D) and E_T values[8] of solvents were found effective for the presentation of relationship between rate and solvent polarity, while other empirical parameters[8] such as X, Y and Z values were unsatisfactory. D values of aqueous alcohol at 25° are 35·5, 52·5, and 68·5 for 80%, 50% and 20% ethanol solutions, respectively. These values were estimated by using data of Koelichen,[9] Amis[10] and Landlt-Boernstein's Table.[11]

Ionization degree of ascorbic acid. The degree of ionization of ascorbic acid (H_2A) or the concentration of ascorbate ion (HA^-), which is the actual reactive species (Eq. 4 or 5), was measured by means of electrical conductance. The degree of ionization is not expressed by K_3 but by K_{obs} in which association of ascorbic acid is also taken into account.

$$K_{obs} = \frac{(fc\alpha)^2}{(1-f)c + fc(1-\alpha)} = \frac{f^2c\alpha^2}{1-f\alpha} \tag{11}$$

Here, f is a fraction of monomolecular H_2A, $1 - f$ is a fraction of associated H_2A, α is the ionization degree of H_2A and c is the stoichiometric concentration of H_2A. The value of $f\alpha$ in Eq. 11 is given by the ratio of electrical equivalent conductance at concentration c (Λ_c) to that at infinite dilution (Λ_0). It is difficult to obtain Λ_0 by the ordinary methods because of poor solubilities of salts of H_2A in organic solvents. Therefore, Onsager's theory[12] is appropriate for the estimation of Λ_0.

$$\Lambda_0' = \frac{\Lambda_c + \sigma c^{\frac{1}{2}}}{1 - \theta c^{\frac{1}{2}}} \tag{12}$$

Here, σ and θ are constants characteristic of solvents (the values of constants are shown in Table 1).

Values of Λ_0' in Eq. 12 were measured at various concentrations of ascorbic acid (c) and extrapolated to infinite dilution, i.e. $c = 0$. The value of Λ_0 or Λ_0' at infinite dilution is presented in Table 1.

TABLE 1. SOLVENT CONSTANTS (σ AND θ) AND IONIZATION DEGREE ($\simeq f\alpha$) OF $2{\cdot}3 \times 10^{-2}$M ASCORBIC ACID AT 25°

Solvent	σ *	θ †	Electrical equivalent conductance (Ω^{-1})		$f\alpha$
			Λ_c	Λ_0	
H_2O	60·2	0·229	17·5	488	$3{\cdot}52 \times 10^{-2}$
Ethylene glycol	4·43	0·669	0·15	68·3	$2{\cdot}20 \times 10^{-3}$
DMF	97·14	0·691	0·153	109·0	$1{\cdot}40 \times 10^{-3}$
MeOH	156·1	0·923	0·14	386·0	$3{\cdot}63 \times 10^{-4}$
EtOH	89·7	1·33	0·052	397·3	$1{\cdot}31 \times 10^{-4}$

* $1^{\frac{1}{2}}\,\Omega^{-1}\,\mathrm{mol}^{-\frac{1}{2}}\,\mathrm{cm}^2$.
† $1^{\frac{1}{2}}\,\mathrm{mol}^{-\frac{1}{2}}$.

The combination of Eqs 10 and 11 leads to Eq. 13.

$$\mathrm{d[DA]/d}t = \frac{3}{2}\frac{f\alpha}{1 - f\alpha}[\mathrm{H_2A}]\,[\mathrm{Cu}]_T k_{14} K_{14} \tag{13}$$

where

$$k_{14}K_{14} = k_4K_4 + k_5K_5p \tag{14}$$

The combination of Eqs 2 and 13 gives the rate constant k.

$$k = \frac{3}{2}\frac{f\alpha}{1 - f\alpha}[\mathrm{Cu}]_T k_{14} K_{14} \tag{15}$$

The solvent effect on the ionization degree of ascorbic acid was examined by plotting $\log f\alpha$ *vs* $1/D$ or E_T which corresponds to the solvent polarity and is shown in Fig. 3 as dotted lines. It is apparent from Fig. 3 that the solvent effect on the ionization step (Eq. 3) is more remarkable than the other steps. No effect of ionic

strength is found in an aqueous solution on addition of KNO_3,[2] and this fact may suggest that the solvent effect on Eqs 4b and 5b is small.

Effect of partial pressure of oxygen. Each constants k_4, K_4, k_5 and K_5 could not be estimated independently, but $k_{14}K_{14}$ values for reactions in various solvents were estimated by means of Eq. 15 to be $1{\cdot}05 \times 10^2$ for H_2O, $2{\cdot}96 \times 10^2$ for ethylene glycol, $5{\cdot}11 \times 10^2$ for DMF, $1{\cdot}18 \times 10^3$ for MeOH and $8{\cdot}41 \times 10^2$ for EtOH.

Ratio of k_5K_5 to k_4K_4 is also obtained with variation of oxygen pressures (p). Experiments were done in water and ethylene glycol with a mixture of oxygen and nitrogen keeping the initial total pressure in the reaction vessel to be 1·0 atm, which was the sum of partial pressures of oxygen, nitrogen and vapourized solvent. The results are shown in Fig. 4.

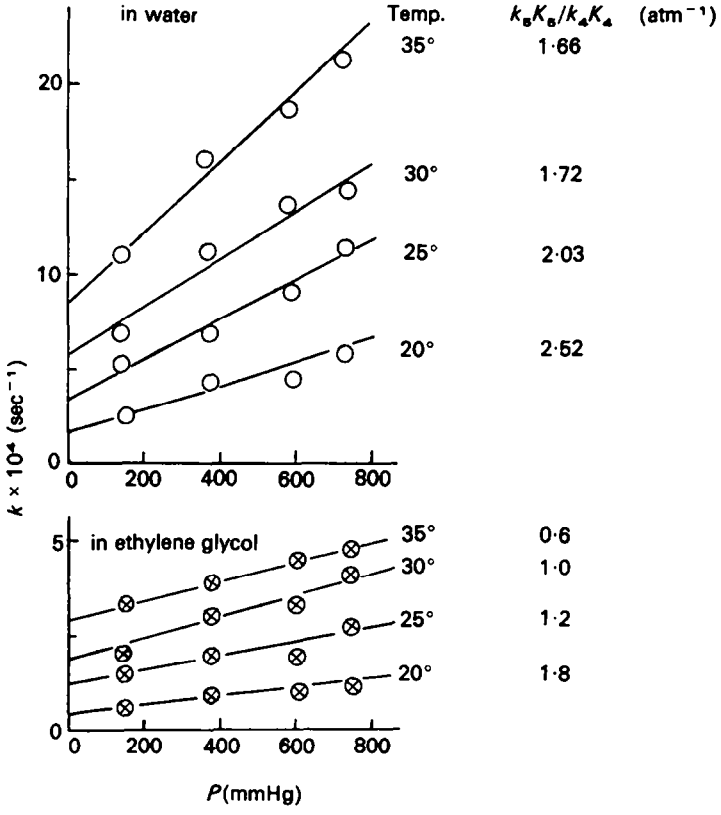


FIG. 4 Effect of partial pressure of oxygen (p), and values of k_5K_5/k_4K_4; ○ in water, ⊗ in ethylene glycol.

The observed linearity between the partial pressure of oxygen and k suggests that Eqs 4b and 5b occur simultaneously, and an equilibrium between these two complexes, i.e. one with oxygen molecules and the other without it, would exist as follows.

$$[\mathrm{HACu(II)}]^- \underset{-O_2}{\overset{O_2}{\rightleftharpoons}} [\mathrm{HACu(II)O_2}]^- \qquad (16)$$

The ratio, k_5K_5/k_4K_4 in Fig. 4 was calculated by the ratio of the slopes to the intercepts of lines. The decrease of the ratio with temperature implies the shift of the equilibria of Eqs 5a and 16 to the left sides. Both k_5K_5 and k_4K_4 are affected by partial pressure of oxygen and temperature more in water than in ethylene glycol. This is consistent with the decrease of $k_{14}K_{14}$ value (i.e. the stability of complex) with an increase of solvent polarity under the same conditions.

Activation parameter. Rate constants at various temperatures gave Arrhenius plots which give apparent energies of activation; 15·1 and 14·7 kcal mol^{-1} for the reactions in water and in ethylene glycol, respectively (Fig. 5). These values are very close to the value (14·4 kcal mol^{-1}) in aqueous solution at 30–45°.[2]

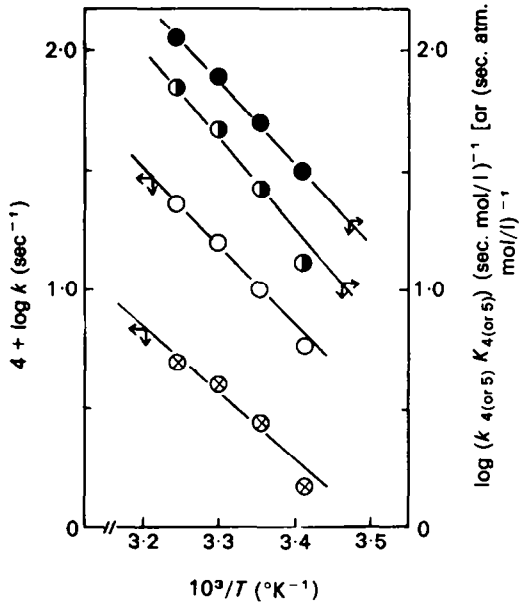


FIG. 5 Arrhenius plots for the reaction in water (—○—) and in ethylene glycol (—⊗—), and the effect of temperature on k_4K_4 (—◑—) or k_5K_5 (—●—).

Using values $k_{14}K_{14}$ and similar treatment, $\log k_5K_5$ or $\log k_4K_4$ *vs* $1/T$ was plotted for the reaction in the aqueous solution, the plots being shown in Fig. 5 (● and ◑). These two lines have the same slopes as obvious in Fig. 5. This may mean that both pathways (4a–4b) and (5a–5b) are possible, the energy barriers being similar. This is another proof for the mechanism of Eq. 3–7.

EXPERIMENTAL

Materials. Ethylene glycol (b.p. 197°), DMF (b.p. 152·5°), MeOH (b.p. 64·6°), EtOH (b.p. 78·3°) and n-BuOH (b.p. 117°) were dried and fractionated by ordinary methods and qualified by the measurements of electrical conductances. Other reagents were of the same grade as in the previous report.[2]

Kinetic procedure. The consumption rate of O_2 was measured by the manometric method[2] and stoichiometric Eq. 1 afforded the concentration of remaining ascorbic acid at time t, $[H_2A]$. The values of $[H_2A]$

at various times during the oxidation were also confirmed by UV spectrophotometry. The first-order kinetic law with ascorbic acid (Eq. 2) was satisfied.

UV spectrophotometry.[7] The reaction mixture at time t was diluted to ca. 5×10^{-5}M ascorbic acid with a buffer consisted of a mixture of 0·4M KCl and 0·4N HCl and its absorbance at 244 mμ ($\log \varepsilon = 4$) was determined at 20°. It was confirmed that the presence of catalyst copper salts and dehydroascorbic acid did not disturb this spectrophotometric estimation.

Electrical conductance measurements. Resistance of an ascorbic acid soln was measured in an usual conductance cell with Pt electrodes (the cell constant of 0·38 cm^{-1}) in *p*-xylene thermostated to 0·05° The combination of an a–c bridge (1000 c/s) and a galvanometer for zero point indicator was employed.

Acknowledgement—The authors are indebted to Takeda Pharmaceutical Chem. Ind. Co. for their gift of ascorbic acid, and also to Prof. T. Takahashi and Dr. O. Yamamoto for their aids in electrical conductance measurement.

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